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Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	June 10, 2022
Subject:	Thalomid	**Page:**	1 of 6

Last Review Date: December 8, 2023

Thalomid

Description

Thalomid (thalidomide)

Background
Thalomid (thalidomide) possesses immunomodulatory, anti-inflammatory, and antiangiogenic properties. Studies suggest that the immunologic effects of Thalomid can vary substantially under different conditions but may be related to suppression of excessive tumor necrosis factor-alpha (TNF-α) production and down-regulation of selected cell surface adhesion molecules involved in leukocyte migration. For example, administration of thalidomide has been reported to decrease circulating levels of TNF-α in patients with erythema nodosum leprosum (ENL); however, it has been shown to increase plasma TNF-α level in HIV-seropositive patients. Thalidomide treatment of multiple myeloma patients is accompanied by an increase in the number of circulating natural killer cells, and an increase in plasma levels of interleukin-2 and interferon-gamma. Thalidomide was found to inhibit angiogenesis *in vitro* (1).

Regulatory Status
FDA-approved indications: Thalomid is indicated: (1)

1. For the treatment of patients with newly diagnosed multiple myeloma (MM), in combination with dexamethasone
2. For the acute treatment of the cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL)
    a. Thalomid is not indicated as monotherapy for such ENL treatment in the presence of moderate to severe neuritis.

b. Thalomid is also indicated as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence.

Off-Label Uses: (2)

1. Castleman disease
2. Langerhans cell histiocytosis
3. Rosai-Dorfman disease
4. Kaposi sarcoma
5. Relapsed, or progressive multiple myeloma (MM)
6. Myelofibrosis

Thalomid includes a boxed warning citing embryo-fetal toxicity. If Thalomid is used during pregnancy, it may cause birth defects or embryo-fetal death. Thalomid should never be used by females who are pregnant or who could become pregnant while taking the drug. Because of this toxicity and in an effort to make the chance of embryo-fetal exposure to Thalomid as negligible as possible, Thalomid is approved for marketing only through a special restricted distribution program: Thalomid REMS program (1).

Thalomid also contains a boxed warning regarding the increased risk of venous thromboembolism. This risk increases significantly when Thalomid is used in combination with standard chemotherapeutic agents including dexamethasone. Patients and physicians are advised to be observant for the signs and symptoms of thromboembolism (1).

Additional warnings for Thalomid are increased mortality in patients with MM when pembrolizumab is added to a thalidomide analogue and dexamethasone, drowsiness and somnolence, peripheral neuropathy, dizziness and orthostatic hypotension, neutropenia, thrombocytopenia, increased HIV viral load, bradycardia, severe cutaneous reactions, seizures, tumor lysis syndrome, contraceptive risks, and hypersensitivity (1).

The safety and effectiveness of Thalomid in pediatric patients less than 12 years of age have not been established (1).

Related policies

Pomalyst, Revlimid

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Thalomid may be considered **medically necessary** if the conditions indicated below are met.

Thalomid may be considered **investigational** for all other indications.

Prior – Approval Requirements

Age 12 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Multiple myeloma (MM)
    a. Patient has newly diagnosed multiple myeloma **OR** relapsed or progressive multiple myeloma
    b. Used in combination with dexamethasone
2. Erythema nodosum leprosum (ENL) **AND ONE** of the following:
    a. Used for the acute treatment of the cutaneous manifestations of moderate to severe ENL
    b. Used as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL
3. Castleman disease
4. Langerhans cell histiocytosis
5. Rosai-Dorfman disease
6. Kaposi sarcoma
7. Myelofibrosis

AND ALL of the following:

a. Patient and prescriber must be enrolled and compliant with the Thalomid REMS program
b. Females of reproductive potential **only**: patient must have **TWO** negative pregnancy tests before initiating Thalomid
c. Females of reproductive potential **only**: patient will be advised to abstain continuously from heterosexual sexual intercourse or to use **TWO** methods of reliable birth control simultaneously for 4 weeks prior to initiation of Thalomid therapy, during therapy, during dose interruptions, and continuing for 4 weeks following the last dose

d. Males with female partners of reproductive potential **only**: patient will be advised to use a latex or synthetic condom during any sexual contact while on treatment with Thalomid and for 4 weeks after the last dose, even if they have undergone a successful vasectomy
e. Prescriber agrees to monitor for signs and symptoms of thromboembolism

Prior – Approval *Renewal* Requirements

Age 12 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Multiple myeloma (MM)
    a. Used in combination with dexamethasone
    b. **NO** disease progression or unacceptable toxicity
2. Erythema nodosum leprosum (ENL) **AND ONE** of the following:
    a. Used for the acute treatment of the cutaneous manifestations of moderate to severe ENL
    b. Used as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL
3. Castleman disease
4. Langerhans cell histiocytosis
5. Rosai-Dorfman disease
6. Kaposi sarcoma
7. Myelofibrosis

AND ALL of the following:

a. Patient and prescriber must be enrolled and compliant with the **Thalomid REMS** program
b. Females of reproductive potential **only**: patient will be advised to abstain continuously from heterosexual sexual intercourse or to use **TWO** methods of reliable birth control simultaneously during therapy, during dose interruptions, and for 4 weeks after the last dose
c. Males with female partners of reproductive potential **only**: patient will be advised to use a latex or synthetic condom during any sexual contact while on treatment with Thalomid and for 4 weeks after the last dose, even if they have undergone a successful vasectomy

d. Prescriber agrees to monitor for signs and symptoms of thromboembolism

Policy Guidelines

Pre - PA Allowance

None

Prior – Approval Limits

Quantity 800 mg per day

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Thalomid (thalidomide) is an immunomodulatory, anti-inflammatory, and antiangiogenic medication. It is indicated for use in newly diagnosed multiple myeloma and erythema nodosum leprosum (ENL). Thalomid is also used off-label for Castleman disease, Langerhans cell histocytosis, Rosai-Dorfman disease, Kaposi sarcoma, relapsed or progressive multiple myeloma, and myelofibrosis. Thalomid has a boxed warning regarding embryo-fetal toxicity and venous thromboembolism. Thalomid is approved for marketing only through a special restricted distribution program, the Thalomid REMS program. The safety and effectiveness of Thalomid in pediatric patients less than 12 years of age have not been established (1-2).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Thalomid while maintaining optimal therapeutic outcomes.

References

1. Thalomid [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; March 2023.
2. NCCN Drugs & Biologics Compendium® Thalidomide 2023. National Comprehensive Cancer Network, Inc. Accessed on October 4, 2023.

Policy History

Date	Action
June 2022	Addition to PA
September 2022	Annual review
October 2022	Per FEP, addition of off-label indications: Castleman disease; Langerhans cell histiocytosis; Rosai-Dorfman disease; Kaposi sarcoma; relapsed or progressive multiple myeloma (MM); myelofibrosis. Changed quantity limit to 800 mg per day to account for new indications
December 2022	Annual review and reference update
March 2023	Annual review and reference update
December 2023	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.